

PATENT
09/849,022
Docket 091/005

REMARKS

This paper is responsive to the Office Action dated August 27, 2003 (Paper No. 13), which is the first action on the merits of the application.

Claims 1-12 were previously pending in the application and under examination. Upon entry of this Amendment, claims 4, 7, and 12 are canceled, and claims 13-23 are added. The added claims fall within the group under examination. Accordingly, claims 1-3, 5-6, 8-11, and 13-23 are now pending in the application and under examination.

Applicant gratefully acknowledges that the information provided in the IDS has been considered by the Examiner.

Further consideration and allowance of the application is respectfully requested.

Interview Summary

The undersigned wishes to thank Examiners Thai-An N. Ton and Joseph T. Woitach for the courtesy of a telephone interview on October 2, 2003.

Issues raised in the Office Action were discussed. The undersigned undertook to provide as a Response to the Office Action certain amendments and remarks proposed in the interview.

Claim amendments:

Entry of the claim amendments does not introduce new matter into the disclosure. Support for the new claims may be found at various places in the specification. For example:

Claim 1:	Claim 1 as previously presented, and by the definitions provided on page 7, lines 34-39.
Claims 8-10:	Page 2, lines 34-38; Example 6 (page 37 ff.), and Example 12 of PCT/US01/01030 (WO 01/51616), incorporated by reference on page 1, lines 15-18.
Claims 13-15:	Page 24, lines 3-5
Claim 16:	Claim 11
Claim 17:	Claims 1 and 11

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Claim 18 & 20: Page 20, lines 18-31
Claim 19 & 21: Page 20 line 32, to page 21 line 2
Claim 22 & 23: Page 23, lines 24-28; and Example 6 (page 37 ff.)

The amendments are made to obtain coverage for certain aspects of the invention that are of current commercial interest. Some claims have been amended to specify that the "primate pluripotent stem cells" are "human embryonic stem cells" (previous claim 12). Applicants intend to maintain protection for equivalents of human ES cells to which they are entitled, including but not limited to other pluripotent stem cells obtained or derivable from a blastocyst. Applicant reserves the right to introduce claims to subject matter previously claimed or described in the disclosure in this or any other application.

Double Patenting

The provisional non-statutory double patenting rejection over copending application no. 10/039,956 is acknowledged.

The present application is further along in prosecution than the '956 application, and is expected to issue first. Upon allowance of this application, applicant undertakes to cancel corresponding claims in the '956 application, or otherwise address this issue.

Rejections under 35 USC § 112

Claims 1-7 stand rejected under the enablement requirement of § 112 ¶ 1 as being enabled by the specification for maintaining pPS cells in a culture environment comprising an extracellular matrix component and a nutrient medium, instead of feeder cells, but not other feeder-free conditions.

This concern does not seem to be appropriate for some of the rejected claims. For example, Claim 4 requires that the pPS cells be cultured on a layer of feeder cells that are drug resistant, as exemplified in Examples 4 and 5.

Without necessarily agreeing with the rejection, claim 1 has now been amended to require explicitly that the ES cells be cultured so that they proliferate on an extracellular matrix instead of feeder cells. Embryonic stem cells are by definition undifferentiated (preamble), and it is expressly stated in step b) that they remain undifferentiated after culturing and genetic modification.

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Claims 1, 4, 10, and 11 are rejected under § 112 ¶ 2 for reasons of claim wording. By way of this amendment, claim 4 has been cancelled, and claims 1, 10, and 11 have been reworded in a manner that is believed to overcome the Examiner's concerns.

According to the definitions on page 7, line 34 ff., a cell can be "genetically altered" or "transfected" by introducing into it any polynucleotide for any purpose. As such, the polynucleotide may or may not have an encoding region and a promoter. The skilled reader will know that other useful types of polynucleotides to introduce into the cell include RNAi, vectors capable of integrating into the genome for various purposes, and vectors such as those described in the Bradley patent (cited later in the Office Action) for inactivating endogenous genes by homologous recombination.

The definitions on page 7 also indicate that a genetically altered cell includes not only the cell that was introduced with the polynucleotide initially, but also the progeny that have inherited the polynucleotide (which can be determined, for example, by PCR amplification or phenotypic change). Accordingly, it is not necessary to refer to the progeny in the claims, since progeny are already covered to the extent that they meet the other definitions required.

Withdrawal of the rejections under 35 USC § 112 is respectfully requested.

Prior art rejections

Claims 8-12 stand rejected under 35 USC § 102(b) as being anticipated by PCT applications by Pedersen (WO 97/47734) or Gearhart et al. (WO 98/43679). Claims 8-12 also stand rejected under 35 USC § 103(a) as being obvious over a combination of Thomson (Science 282:1145, 1998), and Bradley et al. (U.S. Patent 5,614,396).

Applicant respectfully disagrees. For a prior art reference to be patent defeating, it must place the invention sought to be patented in the hands of the public without benefit of hindsight reconstruction of the patent application under consideration. "In order to render a claimed apparatus or method obvious, the prior art must enable one skilled in the art to make and use the apparatus or method." *Beckman Instruments, Inc. v. LKB Produkter AB*, 13 USPQ2d 1301 (Fed. Cir. 1989).

The suggestion in the Pedersen reference referred to in the Office Action does not include any of the features provided in the present disclosure that allow embryonic stem cells to be genetically modified while still maintaining the undifferentiated phenotype. Specifically, it does not disclose the feeder-free culture method of this invention that allows genetically modified cells to be selected from the culture after transfection. As such, the reference does not enable the public to make the invention claimed in the current application, and cannot adequately support a rejection under 35 USC § 102.

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The Gearhart disclosure describes only the production and use of embryonic germ cells. Claims 8-10 have been amended to refer to undifferentiated embryonic stem cells, which are not embryonic germ cells (see U.S. Patent 5,843,780, describing primate ES cells; versus 6,090,622, describing human embryonic germ cells).

Claims 8-10 have also been amended to refer to a cell population *as a whole*, rather than just an individual cell. In view of the fact that human ES cells differentiate so readily (U.S. Patent 5,843,780), the Office has not shown how the skilled reader would know to transfect populations of ES cell and prevent them from differentiating, using any of the prior art methods. Furthermore, cell populations that were being cultured on ordinary feeder cells in the manner of Thomson, before or after transfection, would still contain non-human cells (i.e., the mouse feeder cells), which takes them outside the scope of the claims as amended.

Accordingly, claims 8-10 and dependent claim 11 are patentable over the cited references. Claim 12 has been cancelled.

Claim 11 stands rejected under 35 USC § 102(b) as being anticipated by genetically modified differentiated cells reported in Dey et al. (Proc. Natl. Acad. Sci. USA 273:24095, 1998).

Claim 11 has been amended to place it into process format. This distinguishes it from the Dey reference, since the reference does not suggest or enable the making of genetically modified differentiated cells from human ES cells. Claim 11 is patentable over all the prior art of record, because it is a method claim which depends from and incorporates the limitations of claim 10, which is patentable for reasons already stated.

Claim 4 stands rejected under 35 USC § 103(a) as being obvious over a combination of the Thomson article, the Bradley patent, and an article by Tucker et al. (Nucl. Acids Res. 25:3745, 1997).

Applicant does not agree that there is motivation to combine three references in the manner indicated, or that the combined references place the invention in the hands of the public. Nevertheless, claim 4 has been cancelled, rendering this rejection moot. Applicant reserves the right to reintroduce claims to this subject matter at a later time in this or any other application.

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Request for Interview

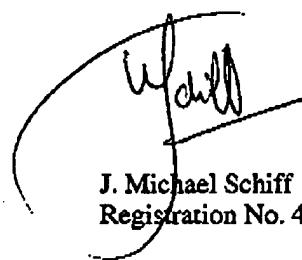
Applicant respectfully requests that all outstanding rejections be reconsidered and withdrawn. The application is believed to be in condition for allowance, and a prompt Notice of Allowance is requested.

In the event that the Examiner determines that there are other matters to be addressed, applicant hereby requests an interview by telephone.

Fees Due

Applicant believes that no fee is required with respect to the amendments to the claims. Twenty claims and five independent claims were previously paid for. Should the Patent Office determine that an extension of time or any other relief is required for further consideration of this application, applicant hereby petitions for such relief, and authorizes the Commissioner to charge the cost of such petitions and other fees due in connection with the filing of these papers to Deposit Account No. 07-1139, referencing the docket number indicated above.

Respectfully submitted,



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